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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,660	06/02/2006	Giovanni Cotticelli	59130-8011.US01	2261
22918	7590	10/29/2007		
PERKINS COIE LLP P.O. BOX 2168 MENLO PARK, CA 94026			EXAMINER BLAND, LAYLA D	
			ART UNIT 1623	PAPER NUMBER
			MAIL DATE 10/29/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/575,660	<b>Applicant(s)</b> COTTICELLI ET AL.	
	<b>Examiner</b> Layla Bland	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>4/14/2006</u> | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This application is a national stage entry of International Application No. PCT/EP04/11494, filed October 13, 2004, which claims benefit of Italian Application No. M12003A001994, filed October 15, 2003. Claims 1-11 are pending in this application and are examined on the merits herein.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-6, 9, 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9 recite the limitation "less than  $-5^{\circ}\text{C}$ ," which is indefinite because there is no lower limit recited and the skilled artisan would not be apprised of which temperatures would be effective to practice the invention as claimed.

Claim 11 recites the limitation "less than  $-10^{\circ}\text{C}$ ," which is indefinite because there is no lower limit recited and the skilled artisan would not be apprised of which temperatures would be effective to practice the invention as claimed.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board

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of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 4 recites the broad recitation "trialkyl phosphate is selected from trimethyl phosphate and triethyl phosphate", and the claim also recites "preferably triethyl phosphate," which is the narrower statement of the range/limitation. Claims 5, 6, 10, and 11 recite similar narrow limitations that fall within broad limitations.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blumbergs et al. (WO 92/00312, January 9, 1992, PTO-1449 submitted April 14, 2006).

Blumbergs et al. teach a process for the preparation of fludarabine phosphate. Fludarabine was dried to give essentially anhydrous material. Phosphorous oxychloride (523 mmol) was added to cold (0°C) trimethylphosphate (1L) and the solution was kept for 1 hour. Dried fludarabine was added with stirring to that solution. After stirring for a number of hours at 0°C, 8 L of methylene chloride was added to the solution. The methylene chloride was removed by decantation to leave a residual gummy mass. Fludarabine phosphate was obtained from the gummy mass after purification. [page 3, line 20 – page 4, line 16] The appearance of a gummy mass in the methylene chloride solution is considered to be a precipitation.

Blumbergs et al. do not teach the reaction at a temperature less than -5°C or -10°C. Blumbergs et al. also do not teach the claimed molar amounts of trialkyl phosphate or solvent.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out the reaction of Blumbergs et al. at temperatures less than -5°C or -10°C. The skilled artisan would have been motivated to do so and would have had a reasonable expectation of success because the reaction of Blumbergs et al. involves a precipitation of crude product from methylene chloride, and one of ordinary skill in the art would realize that lower temperatures facilitate precipitation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust the amounts of trialkyl phosphate used and solvent used by Blumbergs et al. The skilled artisan would have been motivated to reduce the amounts of solvent and trialkyl phosphate used because the reaction involves a

precipitation, and the skilled artisan would realize that large amounts of solvent and/or excess reagent would impede precipitation. It is well-established that merely selecting proportions and ranges is not patentable absent a showing of criticality. In re Becket, 33 USPQ 33 (CCPA 1937). In re Russell, 439 F.2d 1228, 169 USPQ 426 (CCPA 1971).

Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blumbergs et al. (WO 92/00312, January 9, 1992, PTO-1449 submitted April 14, 2006) in view of Wikipedia (Solvent).

Blumbergs et al. teach as set forth above.

Blumbergs et al. do not teach the use of hydrocarbon solvents or toluene.

Wikipedia teaches that dichloromethane and hydrocarbon solvents such as hexane, benzene, and toluene are all nonpolar solvents.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize hydrocarbon solvents such as toluene instead of dichloromethane in the method taught by Blumberg et al. These are all nonpolar solvents and the skilled artisan would understand that they could be used interchangeably.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA)

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1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

It is noted that claim 3 appears to be a substantial duplicate of claim 1. Claim 3 is drawn to the process of claim 1, characterized in that the short-chain trialkyl phosphate is a compound of the formula  $(RO)_3PO$  wherein R is an alkyl radical having from 1 to 4 carbon atoms. "Short-chain trialkyl phosphate" is already defined as such on page 3 of the specification; thus claim 3 appears to be a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

### **Conclusion**

No claims are allowed.

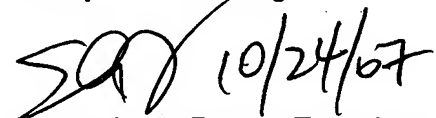
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Bland whose telephone number is (571) 272-9572. The examiner can normally be reached on M-R 8:00AM-5:00PM UST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Layla Bland  
Patent Examiner  
Art Unit 1623  
October 23, 2007

Shaojia Anna Jiang



Supervisory Patent Examiner  
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October 23, 2007